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AP/Gen.

DRAFTSHALL

IG. S SUBCLASS

MAQTQGTRRKVCYYYDGDVGNYYYGQGHPMKPHRIRMTHNLLLN

YGLYRKMEIYRPHKANAEEMTKYHSDDYIKFLRSIRPDNMSEYSKQMQRFNVGEDCPV **FDGLFEFCQLSTGGSVASAVKLNKQQTDIAVNWAGGLHHAKKSEASGFCYVNDIVLAI LELLKYHQRVLYIDIDIHHGDGVEEAFYTTDRVMTVSFHKYGEYFPGTGDLRDIGAGK** TIKGHAKCVEFVKSFNLPMLMLGGGGYTIRNVARCWTYETAVALDTEIPNELPYNDYF **EYFGPDFKLHISPSNMTNQNTNEYLEKIKQRLFENLRMLPHAPGVQMQAIPEDAIPEE** SGDEDEDDPDKRISICSSDKRIACEEEFSDSEEEGEGGRKNSSNFKKAKRVKTEDEKE **GKYYAVYPLRDGIDDESYEAIFKPVMSKVMEMFQPSAVVLQCGSDSLSGDRLGCFNL** KDPEEKKEVTEEEKTKEEKPEAKGVKEEVKLA (SEQ ID NO:1)

FIG. 1A

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(SEQ ID NO:2) tgagaacaca atggcgcaga aattactatt ttgctgctca gctgaggaga ccagataaca ccagtattcg gctgtgaaac catgcaaaga ctggaactgc gacggcgtgg tatggagagt tattatgctg ttcaagccgg tgtggctcag ggtggttaca gatacggaga ttcaagctcc aagatcaaac acgcaggcga cctgacaagc tccgattctg cacgccaagt aagagagtca gaagaggaga ttggcctgaa บ teggtcatec ggcgagcaag gactcataat ctccatccgt tgtggcaagt tcaccatggt caaagacaag tgaggccatt ggtcttacag tatcaaagga gctgggaggc ggaagagttc aggaatcacc ggatgttgga caaagccaat tgaggactgt gggcctgcac cttggccatc cttcataag tgtggccctg tggaccagat gtacctggag tggggtccaa cgaagacgac caaaaagcc ggaggccaag tttctttccc tgtctcccac cacgcgggga ctagtgcggt atgagacagc aggagaagaa gggtcaagga actacgacgg gaatccgcat atcgccctca ctggtggttc tgactgtgtc acgagtccta acacgaatga gtccctcacg aattcttgcg tcaacgttgg attgggctgg atgatatcgt acattgatat ccggggctgg tcaatctatc ctatgctgat ttgaatactt cgcacgcacc gcgatgagga ttgcctgtga cttccaactt ctggtgctgc cggggtagac ttcctgctga gtctgttact aagcctcacc atcgccgtga tgttacgtca ctgtacattg gaccggggtca ctacgggata gggattgatg atgttccagc tttaacctgc agaatgctgc gaggagagtg aaagacccag gaagccaaag atggaaatct gactacatta atgcagagat cagttgtcta ttaggttgct tgctggacat aatgactact actaaccaga gacaaacgaa cgcaagaact tctctgcccg ctctgtcact ccggaggaaa ccacccaatg ctaccgaaaa gcagacggac atctggcttc ccagagggtg ctacaccacg aactggggac gctccgagac tggggatcgg tgtcaagagc cgttgcccgg gcttccatac agagggggc tgaaaaagag ggagaagcca cagctctggc ccacagcgat cagcaagcag tgagttctgt agtaatggag ttccaatatg tgagaacctt cgccatccct ctgctcctct atgtctgggg gcctgagcgr aaacagagga aaaccaagga cgcagggcac tgaccaagta tgtcggagta ttaataagca agtccgaggc taaagtatca acttcccagg ttaactaccc actccctatc tccctaatga acatcagtcc ttcctgagga atggacaagg actatggtct atggcctgtt aagaggcctt tcatgtccaa gtgtggaatt ccattcgtaa agcgactgtt gcatctcgat aagaggaggg tggacctctc 61 181 601 1081 1141 1201 1261 1321 1441 1501 121 241 301 361 481 541 661 721 781 841 901 961 1021 1381

FIG. 1B

The state and states a series of the series

3/38

NYGLYRKMEIYRPHKATAEEMTKYHSDEYIKFLRSIRPDNMSEYSKQMHIPFNVGEDCP LTVKGHAKCVEVVKTFNLPLLMLGGGGYTILRNVARCWTYETAVALDCEIPNELPYNDY **AFDGLFEFCQLSTGGSVAGAVKLNRQQTDMAVNWAGGLHHAKKYEASGFCYVNDIVLA** KGKYYAVNFPMCDGIDDESYGQIFKPIISKVMEMYQPSAVVLQCGADSLSGDRLGCFN FEYFGPDFKLHISPSNMTNQNTPEYMEKIKQRLFENLRMLPHAPGVQMQAIPEDAVHE **ILELLKYHQRVLYIDIDIHHRGDGVEEAFYTTDRVMTVSFYGEYFPGTGDLRDIGAG** DSGDEDGEDPDKRISIRASDKRIACDEEFSDSEDEGEGGRNVADHKKGAKARIEED KKETEDKKTDVKEEDKSKDNSGEKTDTKGTKSEQLSNP (SEQ ID NO:3) MAYSQGGGKKKCKVCYYYDGDIGNYYYGQGHPMKPHRIRMTHNLLL

FIG. 2A

IRAFTSMA!

ttcaaatggg ttatgaagca

tgtatttatt gattttctaa

tttattgtga

ctgggcaagt gctttatgtg

tatactactt

ggcttcattt ttttgttttt tctccaccat

gaagacttct actttttcgt aaatttcttt gtcaaaaaa

1741 1801 1861

1921 1981

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MAKTVAYFYDPDVGNFHYGAGHPMKPHRLALTHSLVLHYGLYKK

CECVEYVKSFNIPPLLVLGGGGYTVRNVARCWTYETSLLVEEAISEELPYSEYFEYFAP HPRVLYIDIDIHHGDGVQEAFYLTDRVMTVSFHKYGNYFFPGTGDMYEVGAESGRYYC LNVPLRDGIDDQSYKHLFQPVINQVVDFYQPTCIVLQCGADSLGCDRLGCFNLSIRGH **MIVFKPYQASQHDMCRFHSEDYIDFLQRVSPTNMQGFTKSLNAPNVGDDCPVFPGLFE** FCSRYTGASLQGATQLNNKICDIANWAGGLHHAKKFEASGFCYVNDIVIGILELLLKY **DFTLHPDVSTRIENQSRQYLDQIRQTIFENLKMLNHAPSVQIHDVPADLLTYDRTDE** ADAEERGPEENYSRPEAPNEFYDGDHDNDKESDVEI (SEQ ID NO:5)

FIG. 3A

ASS SUB

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DRAFTS. IC.:!

acggtctcta ggctctttga aagctttcta tetteeetgg actctctggg ttagtgagga acaatgacaa aaatgttctg ctaagtcggt gcaccatggc gagctggaca gccgcttcca aaggcttcac acaacaagat ttgaggcctc agtaccaccc tgaacgtgcc ttatcaacca gcgttgaata ctgtccgaaa atccagatgt gccagacaat acgtgcctgc gtcctgagga aatttcttt ggtcaccca gaaccatcta gagatacaga ctagcccccc atgaacgggt ttattaataa tccctaacac gctcccgccg ttccactacg catgacatgt accaatatgc acccagctga gccaagaagt gagctgctca ggggttcaag ggaaattact tactactgtc ttccagccgg tgtggagctg catggggaat ggtggttata gaagaggcca ttcacacttc gaccagatcc cagattcatg gaggagaggg ggagaccatg tgtcccaagg gagtcctggg tttggttctc tattagggat gaggcagtcc tttttgaggg ggttctgacc gggctctggc gaggatatga atccaataaa gtgtttcccg gtcctgcatt ID NO: 6 tgcggggcct cgtgggcaac ggcctcccaa agtcagccc tcctcccctg ccatagcctg tgactgccca gcaaggagca tctgcaccat tggcatcctg ccatggtgac ccacaaatac gagtggccgc caagcacctt tgtgctccag catccgaggg gctgctggca tgccccagac ccagtatctg acctagtgtc ggccgatgca gttctatgat tgggatgctg gtggctccta ggagaccaca caatggtacc gtgggccctg aacccagaga gatttggaag caagtgtggg gctgggtggt cactgtttt OES) gcgc gcgcgggagg acgaccccga tggcattgac agccatacca acgtaggcga ggaccgatga tccattttac ttgacatcca tcggggcaga accagagtta tgaaccatgc catccaatga gggaaaagga caaggactga attattggca tctgacttcc aagagagaga agtatgtttt tcctgcagag gcgcatctct gggctggtgg acattgtgat cggtgtcctt ccacgtgcat ttaacctcag ctctactcgt atgagacatc tcgagtactt agaactcacg aagagtggct gctccctcg tttagcggcc gaaagagtct atcgtcctca tacattgaca cgggtcatga atgtatgaag ttctaccaac gccgcggcgg gcctatttct cccatcgcc tacattgact aatgccttca cgttacacag gccattaact tatgtcaacg ggcattgatg ttgggctgct ttcaatatcc tgctggacat agtgaatact atcgagaatc ctgaagatgc acctacgaca aggccagagg gtggagattt aagggctgga ctgactctgg ctctctcc tatctgggac tgagattgcc agggaagatg gatgatggga tggctttatg cctttgatgg tttcttccct ggaattcgcg ctccgaggac tegggtgete cctcactgac cacaggtgac ctgtgatcga cagcacccgc actgatttta caaggatagc ccttgcttcc ctgaatccca caagaccgtg taagaagatg caagagtctt gttctgctcg tggcttctgc cctgcgggat tgtcaagagc tgttgcccgc gcttccctat ctttgaaaac gaactatagc ggaaagcgat cacctcttgg ggggctttg ttgcccctta agacaaggac attttttgta ccctatgaag ggtagtggac agacctcctg ctctcacttt ctgtgatatt 61 121 181 241 301 361 421 481 541 661 721 781 841 901 1021 1081 1141 1201 1261 1321 1381 1441 1501 1561 1621 1681 1741 1801 1921 601 961

APPNOY

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MLAMKHQQELLEHQRKLERHRQEQELEKQHREQKLQQLKNKEKG

KESAVASTEVKMKLQEFVLNKKKALAHPNLNHCISSCPRYWYGKTQHSSLDQSSPPQS

GVSTSYNHPVLGMYDAKDDFPLRKTASEPNLKLRSRLKQKVAERRSSPLLRRKDGPVV

TALKKRPLDVTDSACSSAPGSGPSSPNNSSGSVSAENGIAPAVPSIPAETSLAHRLVA

REGSAAPLPLYTSPSLPNITLGLPATGPSAGTAGQQDTERLTLPALQQRLSLFPGTHL

TPYLSTSPLERDGGAAHSPLLQHMVLLEQPPAQAPLVTGLGALPLHAQSLVGADRVSP

SIHKLRQHRPLGRTQSAPLPQNAQALQHLVIQQQHQQFLEKHKQQFQQQQLQMNKIIP

KPSEPARQPESHPEETEEELREHQALLDEPYLDRLPGQKEAHAQAGVQVKQEPIESDE

EEAEPPREVEPGQRQPSEQELLFRQQALLLEQQRIHQLRNYQASMEAAGIPVSFGGHR

PLSRAQSSPASATFPVSVQEPPTKPRFTTGLVYDTLMLKHQCTCGSSSSHPEHAGRIQ

SIWSRLQETGLRGKCECIRGRKATLEELQTVHSEAHTLLYGTNPLNRQKLDSKKLLGS LASVFVRLPCGGVGVDSDTIWNEVHSAGAARLAVGCVVELVFKVATGELKNGFAVVRP PGHHAEESTPMGFCYFNSVAVAAKLLQQRLSVSKILIVDWDVHHGNGTQQAFYSDPSV

LYMSLHRYDDGNFFPGSGAPDEVGTGPGVGFNVNMAFTGGLDPPMGDAEYLAAFRTVV

GGHDLTAICDASEACVSALLGNELDPLPEKVLQQRPNANAVRSMEKVMEIHSKYWRCL

MPIASEFAPDVVLASSGFDAVEGHPTPLGGYNLSARCFGYLTKQLMGLAGGRIVLALE

QRTTSTAGRSLIEAQTCENEEAETVTAMASLSVGVKPAEKRPDEEPMEEEPPL (SEQ ID NO:7)

FIG. 4A

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FIG. 4B-1	FIG. 4B-2	FIG. 4B-3	FIG. 4B-4	FIG. 4B-5
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cgaggttcac	ggagtagcag	—	
cccaccaagc	tgcacctgcg	tcccgcctgc	
gcaggagccc	gaagcaccag	gagcatctgg	
ccgrgrccgr	cgctgatgct	ggaggatcca	
gccacctcc	gtgtatgaca	gagcacgccg	

ccagaggcag	gcaataacag	ctgga	cagctcaa	aagttaca	tgcac	gagttctcca	þ	CC	gggcc	gcgcccc	Ü	gtgg	บ	Gt	ctc	tctgcagcac	gggagtactg	cacaagct	gc	agcag	gccagcccgg	gctctgct	ggccggcgtg	acgggaggtg	agccctcctg	ggccgccggc	acccgcgtct	gacaggcctc	cagccaccc	cctccggggc
tcgccgagtt	agcacatcaa	accagcggaa		gtgaa	atctgaacca	cccttgacca	ggga	aaatc	gcaggaaaga	agagtga	gga	cgcacagact	ccttgcccaa	agcaggacac	acc	acagccctct	tcacaggcct	cccctccat	tgccccagaa	ggagaa	agccaagcga	gtgagcacca	cgcacgcaca	cagagcccc	tcagacagca	cgtccatgga		cgaggttcac	ggagtagcag	agaagacggg
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cgctcaag	acgagca	agatgc	caccgccagg	agg	Ţ	ga	cccagag	gatgacttcc	gcagaa	Ţ	ctccgga	agaaaga	aaggctc	gcctgcct	cccttccc	gagca	tggtctt	ccctccacg	cggcagcacc	tgcagc	ttccagcagc	agccggag	acgagcc	ag	ccgg	tggagcag	Cg	ccac	gtatga	gagcacgccg
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aaatgcgagt gaagcccaca	aacttct	gacagtgaca		gtacgaaaaa		tggac	gtcctgtaca	ctgat	ggcctggacc	cgatcg	gagggccacc	cga	ctgacc	cttgatcctc	atggagaaag	cagc gggg	accgccatgg	ccatgga	gt	b	cgcccaggcc	acacggg	ggcgggt	tgccgaattc	caaacttgat	aaccactcga		gggac	ttgagtt
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	aaa	tttcggagtt	cagagccgag	aggaggacc	acc	cag	6421
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	cttattttcc	ttactggtaa	gtca	なり	tat	ttactctt	30
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	gaacccaggg	tggctgcaag	ttggagcctg	gccctggatt	ຍ	cactgcag	18
	ttgggttttt	ctttacccac	acgtggggct	catggggcac	ಹ	gca	12
	tccaaacacc	acttgagttt	tagaattcta	atcgtcagga	O	tttaaact	90
	tgaaactcat	tcagcattaa	ccgggggcag	ttgccagatg	cctgggaggc	cccggcca	00
	tgcttaggat	cagggagggt	gtggcaaggg	tttcccctcc	gtggtgtgtt	attacgaggg	94
	cactagtagt	taactttcaa	gggctcttt	agaagcccag	ctg	tgtcctag	α
	ctttcctggt	acgattgtgt	agtgacacca	gtcttttcgg	ga	gtgagagg	87
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	tgtttttatt	taattattt	caaag	ttttaccttt	aca	ttcttgct	70
	tcctttctga	taaatcttt	taataatgtc	ttccgaatgg	tttagcaatt	acc	64
	tttacattt	gttttatgaa	aataagcatt	aaagatcctg	tttttcacaa	tgta	26
	ctgttgattt	tataaatttg	tagcaaagaa	tgagttttta	atgtacctaa	gcaca	52
	ctccaagcct	ccgctcccgt	tctaacagaa	ttaattattt	G	tacaagtttg	46
	gcaactaccc	tegecactgg	gccaacacat	atttcagatc	gattggctag	caagct	40
	tcatgttttc	tgattgaaat	ggatcctgat	ttatggaaag	บ	gaa	34
	ggatggcttg	ccctgcaaat	ttgcgaaggt	tgaatgcaga	atatataaaa	tatatata	28
	tatagaaaa	ataatgcatt	taaaatattt	gaaatcttga	tgattcttat	cttac	22
	tccaagctaa	tccaatgtat	taatatatat	tatatatgta	taaataaata	ttttag	16
	tattgcttaa	agcatgaa	taaaagcaag	tgctttttat	cgat	ttgcagtgtt	10
	Œ	gaagcatgtg	atctggtcgt	gagcatctcc	cat	tcacac	04
	ccaaagtgtt	ttaaacgaat	ccaacaaatt	gttttgaagt	cccgttggag	gtggca	98
	gttccaaaaa	aatggaggta	gtttaagaaa	ctttattgct	Ţ	cggcgg	92
	aggggctgca	ctccgggggcc	cagccgtcat	gcacgggcac	Ø	agctggcc	86
	ctggcaccgc	cctggcagtg	gccagccgag	gtttcctgtg	cggtgggaca	cagcaggaat	80
	aaaaaacaaa	atgccttaag	ctgaggaaca	tttctgaagt	g	gtggattttt	74

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NO:8)

H aagaaaag (SEQ gcagggccca gagcgtgttc tctgaagccc cccacgtgcc tcagtttttc gtctgacaca accggcatga tttctgtaaa gggatcctg gtgggggac ggggaggcaa tgtgtagcct gtgttctcc ggcactggct cgccactggg ggaagaaat ttttgatcag aaatatatat gaagaaaat tattcttaag gtcatattaa tatttatgtg tctctcgagt ccttccacgg ttgagaactg ttacttttag ctgtggttta cactttttt atggcagagg ttgtagactt tttattctga cactctttgc cagaacagtg caggttatca agagcattac gttccttcat accctgatga ccgcagcgtg ctttggggaa gagtttattg actgcctgtc ccttttatct gactttttaa tgtgcgagca taacgaagct ctgctattga tgcatcatct ggcctggcag tccagggcag aggccttggg cgctgggact tcaaggtgtt tttcgtaatg ttgcttttct attcttcttt atatagatat ggactgtacg gatggaaatt ttaaacattt atagccctct ttattgaact ccctggtggc attcatggca gctcagtggc agtttgcgtc aaaggactac ttcacagtga agtcgtgaac ttcttcattg cattctctgc tggggaggaa cctctgcaaa tcctttgcaa tttgagggaa tcccgccgtg ggccgtggcc ggccactttg ggaaggacca tgctcattcc agatacaaaa accaataata cttgtgacgg cagctgtgtt aaatgtgctg acagcaagcg gtcagggagg atggactttg atatataaat gaggttgcat aactcggcag ttgtttgttt gattaaaagt ttgcacgcca agggcgggga agaaaataa ctactcagaa ttgttttgtt cctcactggc ctttccgca cactttaagc aggaaaccat ctctggcatt actttccct tccattcccc ccgtggctta atggagacga ccagcttcac gatattataa tttatatccc agcactagca cacagccacg gcattgatac cctacacctg tgacatttgc tccttggcct aacatggact gcgggaccac gacttttat ctgccccgga ggttctggag gtttgcaagg cctcgccgct cttgtgacat ttgcatcgaa gacttgtttg gaggagctgg tctcattcaa tgatttttgc ctttactggt ttttattgta ttatctagca cgccgccgc aaagagtccc tettetggee tcttaccccg tcagctcact gacacactcg tggaccttta tctgacctgc cagcaggcgg ccagggctct ttgaaaatct tgttttatgg ttttaagttt tatacagatt tcccctctca gaaggaggg tttagggaaa gaattttgtt gctaagattt ctcactttgt atgatgggat gcgtctgcag aagcgagcac ccacctgccc ttaattctaa gaaacagtgt tgatttggag ttagctcggc agattggcaa ttttaagcag gtttcatctg tttctttgaa cctcttggcg ctttatattg gaaaaagt gccaggcgag ggcggactcg gtgatgtatg caattatact acggtcttgg gctagcaggc atctgcctcg tgtgggtcct gggagtcagc cacgcccac cccagagte ttacttctt aaagcaagtt aacattcctt tgggcccacg gcctttctgt acaaaacctt aaattgtact gaatacattt 6601 6901 7321 7441 7501 7561 7621 7741 7861 7981 8101 8161 8221 8281 8401 6661 6781 6841 6961 7021 7081 7141 261 7381 7681 7801 921 8041 8341 6721 7201

FIG. 5A

LRQGGTLTGKFMSTSSIPGCLLGVALEGDGSPHGHASLLQHVLL

The state state of the state of

LEQARQQSTLIAVPLHGQSPLVTGERVATSMRTVGKLPRHRPLSRTQSSPLPQSPQAL

QQLVMQQQHQQFLEKQKQQQLQLGKILTKTGELPRQPTTHPEETEEELTEQQEVLLGE

GALTMPREGSTESESTQEDLEEEDEEEDGEEEDCIQVKDEEGESGAEEGPDLEEPGA

GYKKLFSDAQPLQPLQVYQAPLSLATVPHQALGRTQSSPAAPGGMKSPPDQPVKHLFT

TGVVYDTFMLKHQCMCGNTHVHPEHAGRIQSIWSRLQETGLLSKCERIRGRKATLDEI

QTVHSEYIHTLLYGTSPLNRQKLDSKKLLGPISQKMYAVLPCGGIGVDSDTVWNEMHSS

SAVRMAVGCLLELAFKVAAGELKNGFAIIRPPGHHAEESTAMGFCFFNSVAITAKLLQ

QKLNVGKVLIVDWDIHHGNGTQQAFYNDPSVLYISLHRYDNGNFFPGSGAPEEVGGGP

GVGYNVNVAWTGGVDPPIGDVEYLTAFRTVVMPIAHEFSPDVVTLVSAGFDAVEGHLSP

LGGYSVTARCFGHLTRQLMTLAGGRVVLALEGGHDLTAICDASEACVSALLSVELQPL

DELVLQQKPNINAVATLEKVIETQSKHWSCVQKFAAGLGRSLREAQAGETEEAETVSA

MALLSVGAEQAQAAAAREHSPRPAEEPMEQEPAL (SEQ ID NO:9)

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FIG.5B-1

FIG. 5B

attcctggct	tecetgetge	gtgccactcc	acggtaggca	cagagtcccc	aagcagaagc	aggcagccca	ttgctggggg	caggaagacc	caggttaagg	ggtgctggat	caggcgcccc	cctgctgccc	acaggtgtgg	gtgcaccctg
cacatcctct	cgggcatgcc		cagcatgcgg	accgctgccg	gttcctggag	ggagetgeee	gcaggaggtc	tgagagcaca		ggaggagcct	gcaggtgtac	ccagtcctcc	cctcttcacc	gaacacacac
agttcatgag	ggagccccca	agcagagcac	gtgtggccac	ctcagtcctc	agcaccagca	ccaagacagg	tgacggagca	ccacagagag	aggaggagga	ggcccgactt	tgcagccttt	tgggccgtac	ccgtcaagca	gcatgtgcgg
ctgaccggca	gaggcgacg	caggcccggc	acgggtgaac	ctgagccgca	atgcaacaac	aagatcctca	gaggaggagc	cgggagggct	gaggatgggg	gctgaggagg	gcccagccgc	caccaggccc	ccagaccagc	aagcaccagt
gggtggcacg	cgtggcactg	gttgctggag	cccactagtg	gcatcggccc	gcagctggtc	acagctgggc	tgaggagaca	gaccatgccc	ggacgaggaa	cgagagtggt	gttctcagat	cactgtgccc	gaagagcccc	gttcatgcta
ccctgcggca	gcctgctggg	agcatgtgct	acgggcagtc	agctcccgcg	aggccctgca	agcagcagct	ccacccaccc	agggagccct	tggaggagga	acgaggaggg	acaaaaact	tcagcctggc	ctgggggcat	tctacgacac
-	61	121	181	4	301	9	2	α	4	0	661	2		841

FIG. 5B-1

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FIG. 5B-2

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skrnikkgav prsipnlaev kkkgkmkklg yscaclasgs vlrlvdavlg aeirngmaii rppghhaqhs lmdgycmfnh vavaaryaqq gaavvrppgh haeqdaacgf cffnsvavaa rhaqtisgha 1rilivdwdv hhgngtqhmf eddpsvlyvs lhrydhgtff pmgdegassq igraagtgft vnvawngprm gdadylaawh tetiqvhrry wrslrvmkve aggqdmadsm lmqgsrgltd qaifyavtpl pwcphlvavc pipaagldvt qpcgdcgtiq ydsvylhpns 241 khrirrvliv dwdvhhgqgt qftfdqdpsv lyfsihryeq grfwphlkas nwsttgfgqg espgapcrsa ateaelltch saeyvghlra tekmktrelh ressnfdsiy icpstfacaq latgaacrlv eavisgevin rlvlpiayef npelvlvsag fdaargdplg gcqvspegya hlthllmgla sgriilileg avvalcqdqp seaatggatl aqtiseaaig gamlgqttse eavggatpdq ttseetvgga seeavggatl aqtiseaame gatldqttse eapggteliq pgeenllgea enwvclscyq vycgryingh mlqhhgnsgh plvlsyidls awcyycqayv hhqalldvkn rlhaikeqli aaflhvllpv alefqpqlvl vaagfdalqg dpkgemaatp qasvscalea lepfwevlvr stetverdnm eednveesee egpweppvlp iltwpvlqsr stpgqtnset tglvydqnmm nhcnlwdshh pevpqrilri morleelgia grcltitprp dlmettqymn egelrvladt 61 qameedlivg lqgmdlnlea ealagtglvl deqlnefhcl wddsfpegpe dregpssskl vtkkapgpak prlaermttr ekkvleagmg kvtsasfgee tplasstdhq tpptspvqgt tpqispstli gslrtlelgs esqgasesqa agfaqlthll mglaggklil sleggynira laegvsaslh tllgdpcpml gynltsises maactrsilg dppplltlpr pplsgalasi qsppqdssvt fgarfaekee lmlvhsleyi iahqnkfged mphph (SEQ ID:11) 1 mtstggdstt trgrrsrgnp qvgmrdadyi ildqttseda vggatigqtt qgytinvpwn qeglldrcvs 301 421 481 601 721 781 841 901

FIG. 6A

FIG. 6B-1 FIG. 6B-2	FIG. 6B-3	FIG. 6B
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ggcggagtgg	ggattccacc	ctccagtgtc	tctagcggag	cctaatcgtg	tggcttggtg	ggaaggccct	tegetgegtg	cctagaatat
ggcgggatct	caaccggcca	ccctcagga	ctatccccaa	tggaagaaga	tggctggcac	acagcttccc	gcctcctaga	taattcacaa
aaacgctagg	actatgacct	ccccagtcgc	gttccccgct	ggccaagcaa	gctgaagcac	ctctgggatg	atccaggagg	gaggtgatgt
gggctggttg	agcctcctca	taggcagaac	aaagggagcc	gaagaagctc	gaacctcgag	attccattgc	ggagcaactg	tgaaaaggaa
ctgaggagcg	gcaggggcca	agcgaagaag	gaaatattaa	aaggcaaaat	ggatggatct	agttaaatga	atgccatcaa	accoatttac
gggcagtccc	aagaaccgcg	acaaccaggc	acttcgaagc	gtaaagaaga	ggactgcaag	ttggatgagc	gagcggctcc	tcctttcagg
ᆏ	61	121	181	241	301	361	421	481

FIG. 6B-

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6B
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ı	ggatccgctg	ctgcacgggg	ggctttgatg	ggtctcagct	aactggtgct	tttaacccag	2281
Ī	tgcctacgag	tgcttcccat	catcgcctgg	agctgcctgg	υ	tgggtgat	22
	ეგეეეენგნე ე	tggcatggaa	accgtcaacg	cacaggette	daaccacada	gategg	H
	tgccagcagc	gggatgaggg	ttccccatgg	tggcaccttc	gctatgatca	ccctg	10
	gctatatgtg	accccagtgt	tttgaggatg	tcagcacatg	gtaatggaac	tccacc	04
	ggattgggat	tcctgattgt	gccctacgga	cagtgggcat	C B	gctcgccatg	O)
	ggctgtggct	tcaactctgt	tttigctttt	agcttgcggt	agcaggatgc	caccacgcag	92
	tcccccagga	ctgtggtgcg	aatggtgctg	agaggtcctg	tgctctcagg	gtggaggctg	98
	ctgccgcctg	ctggcgctgc	cagcttgcca	cgcctgtgca	ccagtacctt	tatatctgcc	80
	tgactccatc	gttccaactt	caccgtgaga	ccgggagctg	aaatgaaaac	ccac	74
	tcatctccgg	agtacgtggg	cacagtgctg	gctcacctgt	aggctgagct	cctgccacag	Φ
	gacaccgcgc	gcctcaccct	gaaggaaat	gctgggcctt	gtctggagga	atcatgtgcc	62
	catcttgcgg	taccccagcg	caccctgagg	ggacagccac	gcaacttgtg	atgaatcact	26
	ccaaaatatg	tggtctatga	cgcacagggc	gctacagtct	calggccagt	ccaatcctga	20
	ccctgtgctc	cctgggagcc	gaggaaggac	ggagagcgag	acaatgtaga	atggaggagg	44
	gaggacaac	agaccgtgga	agatcaactg	ggttcttgtg	ccttctggga	gcccttgagc	∞
	tgctctggaa	cagtttcctg	gcccaggctt	ctgccggagc	ctggtgccc	ccggagtcac	32
	ttgccccatg	tgggagaccc	cacaccette	tgcttcgctc	aaggcgtcag	gaaatggatg	26
	caacctccgc	agggtggcta	ctgtctctgg	caagctgatc	tggcaggagg	ctcatgggtc	20
	aacccacctg	tegeceaget	ccggcagggt	ggccgccact	agggcgagat	ggggaccca	14
	tgccctgcaa	ctggatttga	ctggtggccg	tcagctggtc	agctccagcc	gtcgccctcg	08
	cctgctgcca	tcctgcacgt	attgctgctt	tgctgactac	ggatgcggga	aaccaggtgg	2
	tgtgccttgg	ataccatcaa	ggccaaggat	tttcggccaa	ccaccacagg	tctaactggt	9
	cctgaaggcc	tctggcccca	cagggtaggt	ccgctacgag	tctccatcca	gtcctctatt	0
	ggaccccagt	ccttcgacca	acacagttca	cggtcaagga	atgtgcacca	gtagattggg	841
	ggtccttatc	gcacccggag	cagaaacacc	ctatgctcaa	tggcagcccg	cacgtggctg	∞
	catgttcaac	atggctattg	agtcttatgg	cgcccagcac	ctggacatca	attaggcctc	2
	catggccatc	tccggaacgg	ggggctgaga	tgaggtaatg	ggctggtgga	tctgtcctca	9
	ggcctcaggc	gtgcctgcct	tcatactcct	gcatccgaac	cagtttatct	acccacgact	0
	cctagcagac	aactccgtgt	aatgaggag	ccagtacatg	tggaaacaac	attgacctga	

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FIG. 6B-3 gttgcatatg ggagccgata gcccaagag gcatggcaag cagctcagtg taactggcag gaaagggggg ggagggagt caagctgtt (SEQ ID NO: agcccagaag aacattggcg taataaagta ccactactcc tcatgaggat

gatgggcctt catctcagag gaccctgcca ccatcgcaga cagttctaag gatgaccaca atttggggaa tcaggaccag aggagctaca gactacgtca cacagaccac agaatctcag tgtgacacca aaattctgga tgaggcccac ctcccactgc ggcagccatt cactccggac ctcagaggat cagtacactg ggctgattcg cctagacgtg ctcttgctat tcaggcctat gtttggggag ttgaggggca ttaatacttt ccacctgct acctgacatc ccatccaagt aaggaccctc cctcggcatc tggccctcac ccatttctga tcgggggagc accagaccac cactggacca agggggcctc tattttatgc accagaacaa cttcaccttc gaggggtagc tatttaagtg catcgcccgc cacccCtgct tagctgagcg aggctgtagg tagcctcgag agatatctcc gtcaggacat ctgcagcagg gggtgtgtct aacaccatgg gttactactg gcccacctca teceectgee ggtggctata ggagacccac atcactgaga gggaaagtca ctggcccaga gccattctgg acctcagagg caaactcctc actacaccc agcgaacctC gatcaggcca tgccccatac tcagcctggc aacatcgccc tacggtccct gaagacagag aaacctaggt acagctgtgg gaggaggctg gagggagcca gcagctggag caagagaact cacatgctcc taccttggat caagagtgct catcaatggc ttccaggctg attgtggatc tgagggttat catgaaggca agcaggcatg tgtgcaggga ggagctaggc ggtggcagta tggaacaatc catcgacctg agccccagaa tgcaactccc tatcctagag atacatactt cctggcctca ccaaccagcc taactcagag gggagccact gaccacctca tgtgggagga gggccagact ggcagccatg cgagctgatc accaggagag gggcctcact agatgtgaag gcgacgatta tcctcagcca ttccagcctg aggtgtcacc ccatctcgga gtggtcgtta aggctctcct acccacacta gaatatcctt gcattatcct cctgcactcg tatcaggggc gcttacgggt agaaggcacc aggttctgga caggccagac cagccacagg tgctgggcca cagaggagac gagccacgct cagggggcac caacctcacc tcaggacctt aggagaacct agggatctag gtccccattc gtgggactg ggggctgcc gccagtggcc tccatggctg cggcccccac tactggcgca ttggtcacca cgagaaaaga gagtccactc ccctcagagg ggggagcca cagaccacct gctgttgggg ctggcccaga gaggaggctc cagaccccc attgggagtc gccccaggag atgctgacgc ctgccctggt acccaacctt caggtctacc cacccgctgg gtccaccacc gatatgcccc gatagaccag atcccatcct taagagaact 3901 3961 4021 4081 2341 2401 2461 2521 2581 2641 2701 2761 2821 2881 2941 3001 3061 3121 3181 3241 3301 3361 3421 3481 3541 3601 3661 3721 3781 3841

kasieelgsv elhssnaarw qlqqqskask gagsgegfnv aplggyhvsa seegwkqkpq dtpmpelgvg gipyrtlepi ${\tt rrknpllrke}$ hptlgprgpi **tpartlpflt** weqqrlagrl pfhfagsimt sakpsekprl rsvepmrlsm lertvhpnsp lrykpkksle agfdaaeghp pilgdsdrrt lkthvqvikr sqarvlssse rsqceclrgr vgvdtdtiwn ffnsvajacr fpgsgavdev 11tvpg1gp1 plaahpavii allgnrvdpl rktvsepnlk 11dpsgshap evilkkqqaa spndsehgpn adhstamgfc hlflaglqqq pgpmqprleq hgqpeargpa pasisapepa rmfemlpcgg slhrhddgnf iwsrlqergl efspdlvlvs icdaseacva assvvkqkla 1ppsatappp hpehagrigs algrpgrlhh ssstpasgcs ddglehrelg lsraqsspaa ngklagiiag favvrppghh alegghdlta psdppehfpl clpsrlqpil fyqdpsvlyi frivvmpiar ID NO:13) aetlgdssps Wplsrtrsep tdgggggwv lplaggghrp tnplsr1kld kvasrelkng vhhgngtqqt pmgdpeylaa mnlaggavvl dpgag (SEQ vepppept11 hkdkskrsav ssflppvpsi phglepeagg hqcscgdnsr gliydsvmlk mdlrvgqrpp sappslrrrp lgsphtplf1 terlsgsglh rqipsaedle prgstgdcvi hserhv11yg aagsvtdlaf askilivdwd nvawaggldp kcfgymtggl etegatrsml pachplaggr pqeqelrqll 181 241 301 361 421 481 541 601 661 721

FIG. 74

FIG. 7B-1	FIG. 78-2
	

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catgagagtg	tatcatgccc	tgccccaggc	ggccagcggc	cagcgcctgc	atgaggctct	ctgcggcagc	aagcagaagc	catcccaaca	acccgctcca	gagcactccc	aagaagtccc	೦೦೦೦ರಿಥೆ೦ರಿ	gcatcagggt	agtgaccgca	acteceetet	ctgcagccca	gggcttgggc	gggtcaggcc	accgctcccc	caggtgatca	gctgaagacc	cacagggagc
gaaaaacccc	gatcaggctg	gtccctaggc	cctgcgggtg	gcagcgtccc	ggtggagccc	ggaacaagag	cagcgtggtc	aagaacagtc	ggaaggagcc	tgaccccca	ccataagccc	gccccccagc	cagcacgccc	cctgggcgac	gagccccac	gccctcccgc	gactgtgccc	gagatatat	ccccagtgcc	aactcacgtc	gataccctcg	cggcccggag
attaagtgag	gctgaggggg	ccctctctct	agcccatgga	tgctggccct	agcagcgctc	tgggaccca	ctgtagccag	cggccctaga	ccctggagac	gcccgcccag	tgaagctgcg	aggagagtgc	caagtagtag	ccaatcccat	caatcctggg	ggggcacctt	ccccgctgct	tgaccaccga	agcccctgcc	agcagctcaa	ggctgcggca	tggtggacga
ccacgacagg	cctgagggag	ttaccctgct	cctcagccgc	gagcccacat	ggcctgcagc	gagttgcagg	aagcgaagtg	aaacagcagg	accccggagc	cctgctccca	gagcccaacc	ctgctccgaa	gactcctccc	gagcacggcc	೦೦೦೦ವಿವಿವಿವಿವಿವಿ	cccgaggctg	ggctctcatg	cagtccttaa	actcgctcag	ccccgcctgg	gagaagcccc	ccgggccagg
ccttgcagga	gtcaagtgag	actttccagt	cacaccaggc	gcccccacca	cttcctagca	gccgacgccc	ggacaagagc	gattctgaaa	tccctacaga	ccttccgcct	gacagtctct	gaagaatcca	gaccctcgga	caatgacagc	gactctgggc	tggcttggag	ggacccctca	ccactttgcc	actgagccgg	ccccatgcag	caagccgagt	tggcggggga
ataataccta	ttttgccatt	ccgaggacaa	cctgcgcaga	ccccagtgga	accaccacct	ccatggacac	ttctccacaa	tagcggaggt	gccccggcat	tgctcagcag	ctctgcgcaa	cggagcggag	ggcccgcaga	gcagtccccc	ggacccatcc	tcctgcccca	ttcctctcct	ccttgccctt	tccactggcc	caccgccggg	agaggtcagc	tggagacaga
Н	61	N	181	4	0	9	2	α	4	601	9	2	∞	4	0	9	02	08	14		1261	1321

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atgacgcagc agggtggatc ctcctgtcca agtgaccgca cctcaggtgt ggggacactg teggteatge ggccgcatcc tgtctccgag gtgctcctct gggctcctgg gacaccatct actgacctcg ccccaggac gccatcgcct attgtagact agtgtgctct gctgtggatg ggaggtctgg acgcccatcg gctgagggtc catgacctca ctctctggag gctggtggag catgcccttg tcttccccag ctctccagct tagagatcct cccagggagc ggagggtggc agcgcctggc cctgggtctt tgacagttat ggcccgagtc gatctatgac tgagcggcac tggcagtgtc tgtggtgcgg caagatcctc ccaagaccc gggagtggg ggcctgggct atttgatgct ttttggatac tctgggtaac atgccactcg aagtggaggc cctcggagca gcccgcccac ccagcagcac gggcagcacc ccgggctcag ggagcacgcc ccagtgtgag gaagctggca caactcagtg gatagtcgtg ggtggacact atggtttcgc tctgcttctt gcaaggccag aaaccttcta atgtcaatgt tgctggcctt tggctgctct cccaacctca ggctgcatgc gacaaagaag gaagataggc ggaaccatct agcccccatt ctgcctgctt acgatactat acttcttccc ctgctttcag tgtctgccgg ctgccaaatg aggtacacta gtggggttgg gctgggccgc ggctccccg ggcctctgtc gcaggcaccc ggcctcggag tggacaacgg ctgccagcca ccacagggct gagctaaaga gccatgggct ggcacccagc gacgacggca gagggcttca ctagtcctgg taccatgttt ggcgcagtgg gaggcctgtg aaacagaaac taaatactgg gccaggggct ccctggcaat agagaacagc gccagaggcc ctggctgggc cgcctcaaac aatgcagccc agcaaggcca gagtacctgg catcctggct ctaaggctct gccccagagc ctgcccttca ggtgacaaca ctgccctgtg ggtgggcacc caggagcggg gagctgcagt (SEQ ID NO:14 ctcttctaac agttggaacc ctatgaatct cctggcagga tgcctagagt acLgggtggc tgacgcctct gggtgcacag tctctgtggg ctctccagac agaaggctgg gcagcccgag acagcagcga tgccaggacc gtgctcctgc gtcccggctg cccctcagc gtttgagatg tcattccLcc ggcttctcgt tcattcaaca gcaacagcag ccatggcaac gcatcgccat tggcagcggt gggggatcct tctggcccag ctcactgtca ctccttggaa บ cccttcaga ctggcgtccc gaggaagaac ggacctggtt gtgggcaagt accegecce aactgatgaa cagccatctg gccgtgatcc accatgcaga aggtaggggc gactcctggg gtgagaaat acgaacatga cagagaccc tgaagcacca gccggaaggc acggcaccaa cacagcggat ggaatgagct ccttcaaagt gccggcagct gggacgtgca acatctcct accccccat cccgagagtt tgggccatgg tgctctggga tgctgcttcc agagcatctg 3061 3001 3121 2881 2941 2521 2581 2641 2701 2761 2821 1441 1981 2041 2101 2161 2221 2281 2341 2401 2461 1501 1561 1621 1681 1741 1801 1861 1921

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scrpdrneph hkqmrivkpk rilyvdldlh ilqwqlatli **yaaaiggati** iqdgiqdeky dcpategifd pvgigkclky lakipkrasm vhslieayal gilrlrrkfe kgryysvnvp gpdyvleitp htdaylqhlq kvsqegdddh pdsieyglgy gfcylndavl tgdvsdvglg gdpmcsfnmt ipdbefftay vyqafnpkav vlqlgadtia tarcwtyltg vilgktlsse ftskvmtvsl hkfspgffpg gnlkhvv (SEQ ID NO:15) gqslvpvyiy speyvsmcds ckvainwsgg whhakkdeas yqicesvlke lggggynlan vasmeematf taaqclidgm riqqilnyik meepeepads hgdgvedafs 181 241 301 361 61 121

FIG. 8A

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			•		_	•			_		_	_			_		.		-	_				_		. .	FIG. 8B
ggaagatgga	atagtcc	gtatggtgca	ctaaagtggc	tccagaaggt	gttatgactg	gatcacago	gagggtggca	tcctgggaat	tgcaccatgg	ccctgcacaa	tagggaaggg	aatattacca	agtggtctt	tgactccagt	catttcggg	ccggggtcat	catatggtcc	ccaccgaat	gacagaaag	ttatgcaag	gaaaatttc	ccagagtcct	aaaaaaca	gggagggg	caccagttt	ggagccc	FIG
gga	tctat	gta	cta	taa	gtt	cga	gag	tac	tgc	CCC	tag	aat	cag	tga	tca	CCG	cat	S	tga	ttt	tga	CCA	taa	tgg	tca	ngt	
ggttttaagc	ccggtttata	aaacgggcca	atagttaagc	ctgcagcatc	tatgggctag	ggaggggcta	aactggtctg	aatgatgctg	gattcggatc	atgaccgtgt	gacgttggcc	caagatgaaa	aatcccaaag	tcctttaaca	ttggcaacac	acatacttga	tttttcacag	cgcaatgagc	gtggtctagt	agacagcgtg	aattacttcc	ggcaggcacc	agttcttatt	ttaagcgaat	atgagagcag	ggaccancca	ID NO:16)
gcacgagaac	gtcgctggtc	caagatcccc	gcaaatgagg	tgatgcttat	ctccatagaa	agcagctata	agtagcaatc	tegttatete	tecetaegtg	ctccaaagtc	tgacgtgtcc	ggatggcata	ccaagccttt	tcccatgtgc	tcaatggcag	tcgatgctgg	agatcatgag	ccggccagac	tctgaagcat	cctataatga	atttgaaaga	ggggtgaaga	ccacatttaa	aaaattattt	cagaagctgg	tngggcctcn	gagg (SEQ 1
gccgaattcg	acagtgggca	actccctggc	cactgcataa	ccttccacac	atcatccgga	ttgactatgc	gaatgtgcaa	catctggttt	ttgagcgtat	tcagtttcac	caggaacagg	tgcccatcca	aggaagtata	tagctgggga	agtacatccc	ccaacacggc	ctgagatccc	cgccaagctg	tcaaagggaa	aggagtggtg	tgcagggaaa	ctggcttcct	aggagatarc	ttaatctttg	tgaaacagat	caggcagggn	ngcagactgg
acgagctcgt	gaaccggcgg	agtatgtgtg	gaagcatatg	gagatggcca	ggcgatgatg	gaagggatat	ctgattgacg	aaagatgaag	cgacggaaat	gaagacgcat	ggatttttcc	agtgtaaatg	agtgtactaa	gccgacacaa	aagtgtctca	tataaccttg	acactatcct	ctggaaatca	ctcaactaca	tccagagctg	aatttgtgac	caagtggcag	taggggaaga	aatgaaattt	tcatcttaaa	aggcagctga	ggtactgatc
gaaattcggc	ggagccggag	cgagtatgtc	ttctttgatt	ctccatggag	cagccaagag	cccagccact	tgcccaatgc	tcatgcaaag	attacgattg	agatggtgta	attctcccca	acggtactac	gatctgcgaa	acagctggga	gggaattggc	aggaggaggc	cctagggaaa	tgattatgtg	ccaacaaatc	agatcaggtt	cagtttgrgg	caaggggcat	caactggacc	cacacacaca	agtattttaa	gtagggcagg	tgggagagan
⊣		121	181	241	301	361	421	481	541	601	661	721	781	841	901	961	1021	1081	1141	1201	1261	1321	1381	1441	1501		1621

The term from the state of all the terms are the terms are

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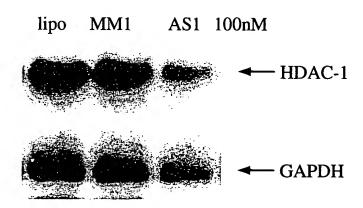


FIG. 9A

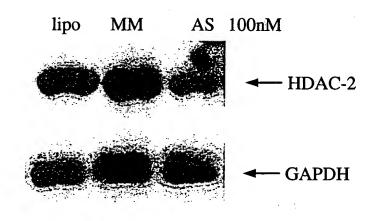


FIG. 9B

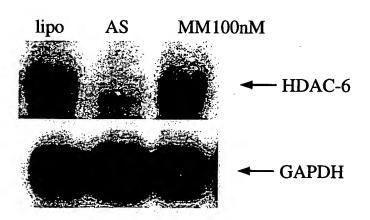


FIG. 9C

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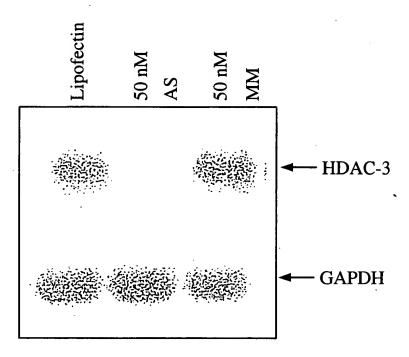


FIG. 9D

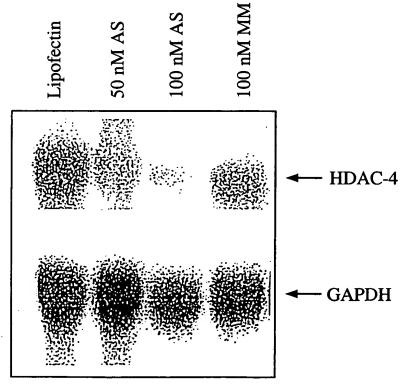


FIG OF

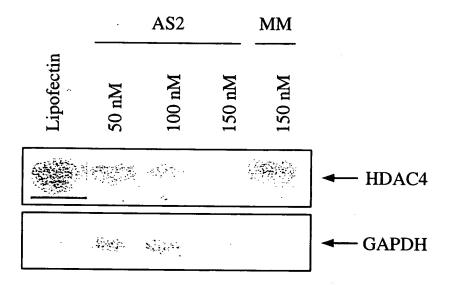
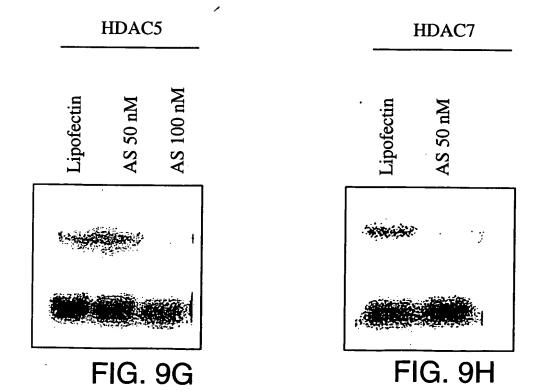
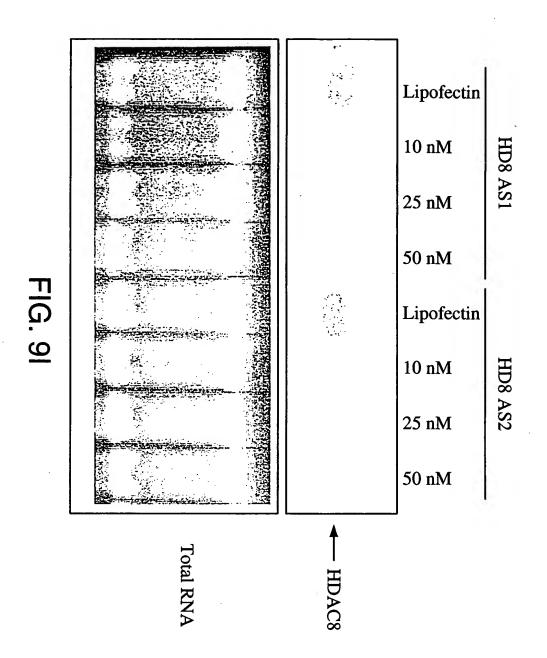


FIG. 9F





	← HDAC-1	← HDAC-2	← HDAC-3	+ HDAC-4	← HDAC-6	← Actin
HDAC-6 MM	October 1					distriction of the second
HDAC-6 AS	4.705.00					AND
HDVC-4 WW 1	1000			A DEPTH	9	(T)
HDVC-4 V2 I	-2127788	4500500m			OPENICED A	The second
HDAC-3 MM		40000		4)242302	/H3467	CO COURSE
HDAC-3 AS	-			Total Control		Carro
HDAC-2 MM	-			***************************************	ACCORAGE OF	Contraction of
HDAC-2 AS	STATE OF					
HDAC-1 MM				esperantes		
HDAC-1 AS 1				-420am	CCRC Lab	ATTACA TO THE PARTY OF THE PART
Lipofectin	None Park					
		· • • • • • • • • • • • • • • • • • • •				<u> </u>

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AS = Antisense
MM = Mismatch
NS = Non-specific control
3 day treatment
Oligonucleotide cone – 50nM

FIG.

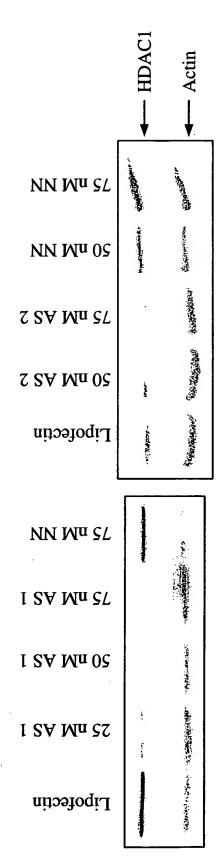
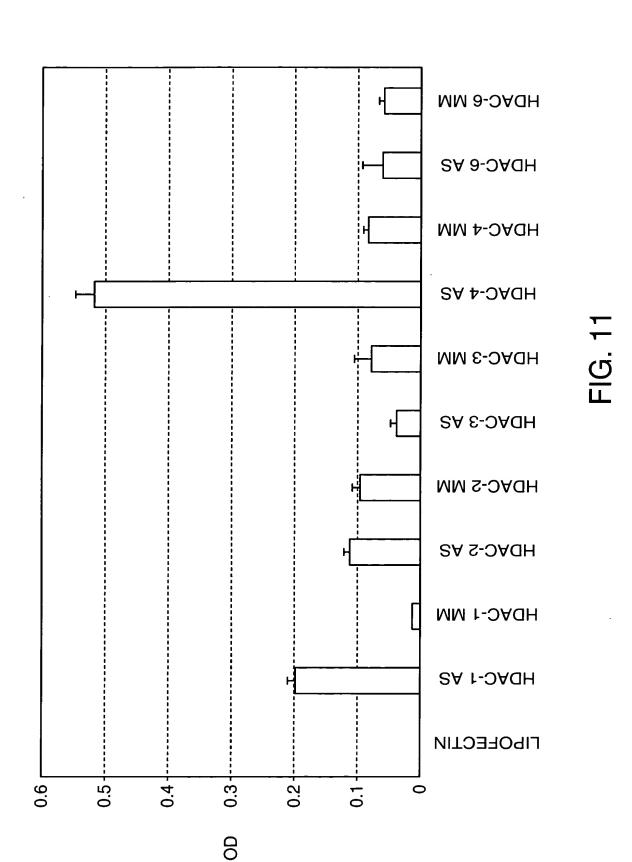


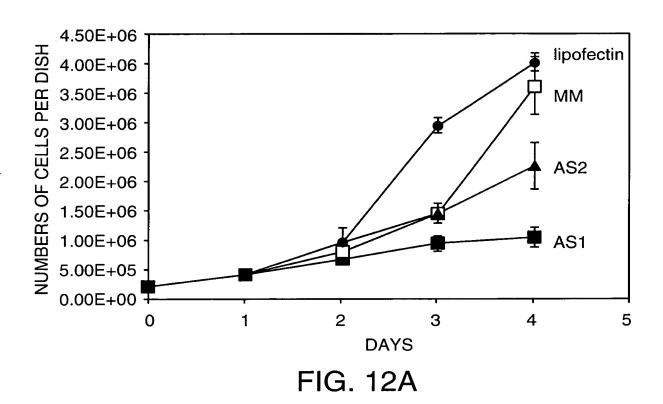
FIG. 10B

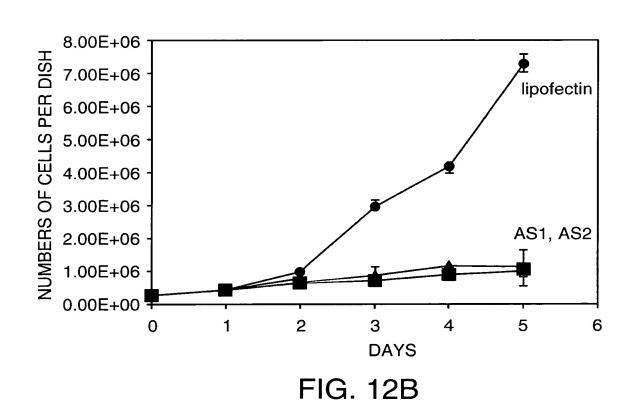
30/38

H. H. H. B. Sa. offers H. H. H. H. Sand

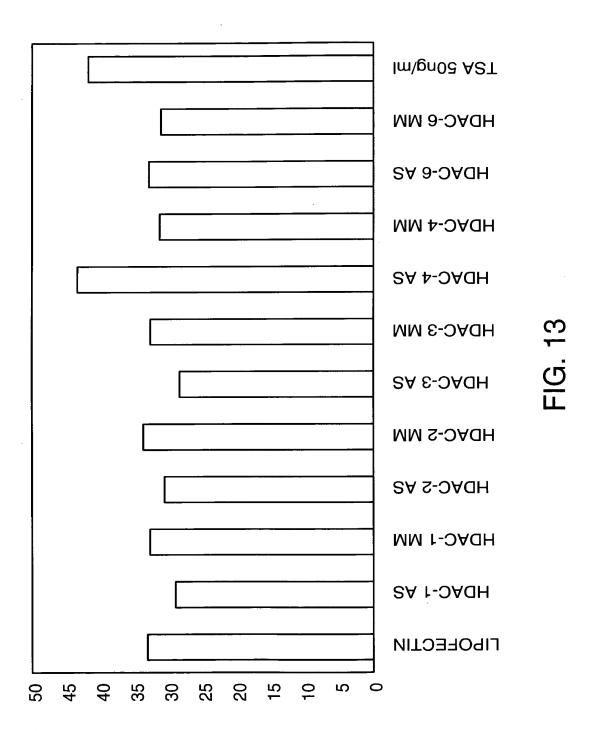


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% OF CELLS WITH DNA CONTENT (>=2N)



C. FIG.

APRIE

Jan 1 Hell of Harm 15 to 15 to

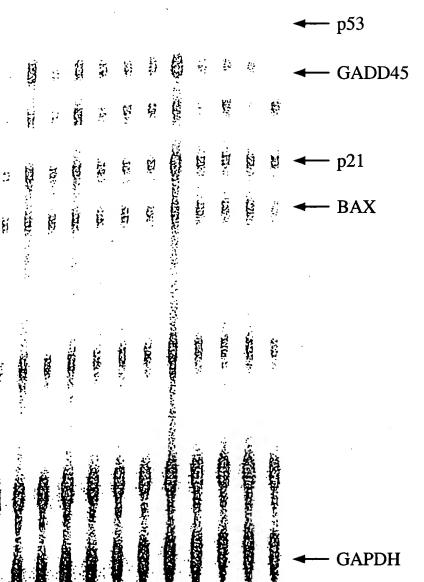
H. U. H. H. H. Harrison and St. Santo

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FIG. 14

- Kalletter Calletter HANNE BELLEVINGER STATES

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			p21	Actin
			1	↓
•		AST		ABOUT AGENCY
	HDAC-6	MM	(CEE)	
	HD/	SA		**
	C-4	MM		
	HDAC-4	SA	44 ZIA	, (20 m)
and grown	LC-3	MM		
	HDAC-3	SA		
	.C-2	MM	CPSEA	down
	HDAC-2	SA		
	C-1	MM	diamo	
	HDAC-1	SA	- C.	
	ctin	eloqi.J	P	

FIG. 15

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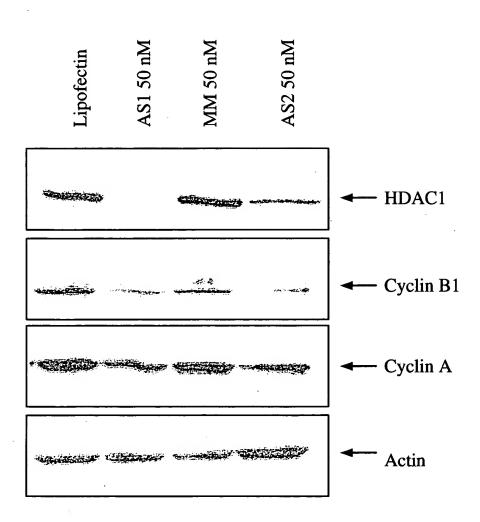
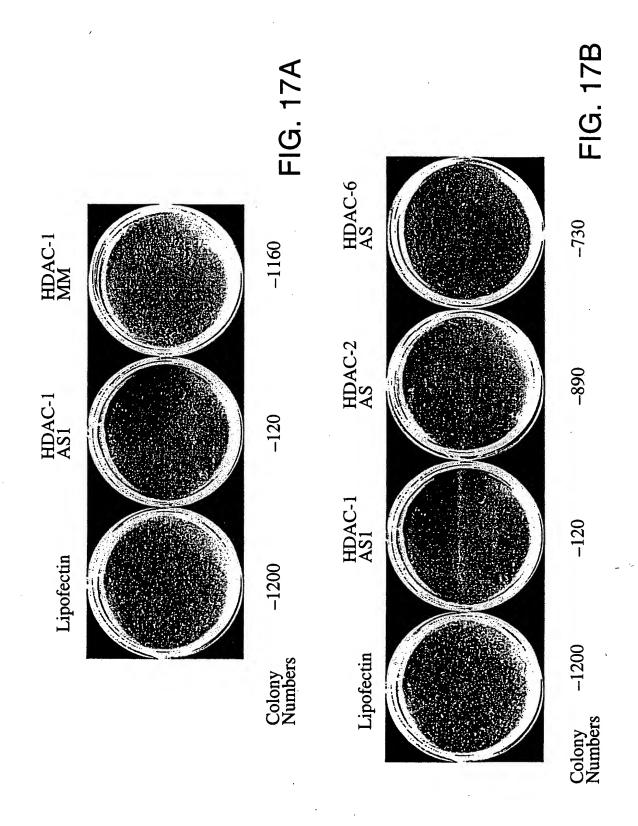


FIG. 16

COMITAL CHECK



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Compound 3

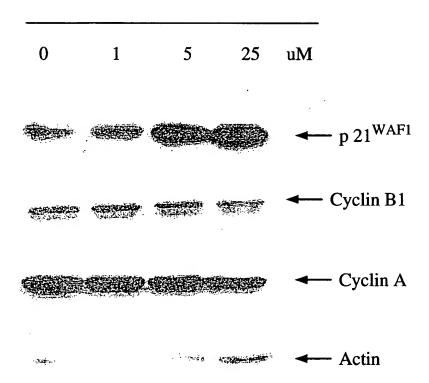


FIG. 18